The Remarks

Applicant thanks the examiner for a thorough review of the claims based on the cited art and for indicating that claim 15 would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims. Claims 1-4, 15, and 24 have been amended, claims 36-43 are new, and claims 1-4, 15, 16, 24, and 36-43 are pending. No new matter has been added by this amendment.

Rejection under 35 U.S.C. §112

Claim 24 stands rejected under 35 U.S.C. 112, first paragraph, for allegedly not complying with the written description requirement. Applicant has amended claim 24 to obviate the rejection and requests that the rejection be withdrawn.

Claims 2-4 stand rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. Applicant has amended claims 2-4 to obviate the rejection and requests that the rejection be withdrawn.

Double Patenting Rejection

The examiner has alleged that claim 16 is a substantial duplicate of claim 1. Applicants traverse the rejection.

As correctly stated by the examiner, claim 1 recites an expression cassette comprising SEQ ID NO:2. The examiner further correctly states that the expression cassette encodes the Factor IX polypeptide set forth in SEQ ID NO:3. However, the examiner is incorrect at stating that the claims are substantially the same, since an expression cassette comprising SEQ ID NO:2 can include more nucleotides in the open reading frame, and claim 16 is limited to expressing a "...polypeptide consisting of...SEQ ID NO:3." (emphasis added) The examiner should appreciate that one skilled in the art may, for example, choose to produce a construct having the Factor IX gene placed between reporter genes to monitor the Factor IX protein. Claim 1 would read on such a construct, whereas claim 16 would not. Accordingly, Applicant respectfully requests that the double patenting rejection be withdrawn for at least this reason.

Rejection under 35 U.S.C. §103

Claims 1-4 and 16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,936,243 ("Snyder") as evidenced by Simonet, et al. J. Clin. Invest. Vol. 94:1310-1319(1994) ("Simonet") and Nguyen, et al. Oncogene 12:2109-2119(1996) ("Nguyen"); and in view of Jallat, et al. The EMBO Journal Vol. 9 (10):3295-3301(1990) ("Jallat") and Kurachi et al., J. Biol. Chem., Vol. 270 (10):5276(1995) ("Kurachi").

According to the examiner, Snyder (as evidenced by Simonet and Nguyen) discloses all of the elements of the claimed invention except for the use of a Factor IX intron in the expression cassette. Jallat and Kurachi are cited for teaching that Intron I, or a fragment of Intron I, can increase the expression of Factor IX. However, only a reference that is prior art under 35 U.S.C. § 102 can be a prior art reference under 35 U.S.C. § 103. See 35 USC § 103 and MPEP § 2141.01(1). And, a statement made by an Applicant that a reference is describing the Applicant's own work will remove the reference from consideration as prior art. See MPEP 2132.01, citing to *In re Katz*, 215 USPQ 14 (CCPA 1982).

Applicant has submitted an *In re Katz* declaration in paragraph 6 of the attached declaration stating that Snyder is not a prior art reference to the pending claims of the present application, since the reference is used against the present application only for the construct that is taught in that patent, and among the other inventors listed with Dr. Kay in Snyder, that construct is attributed soley to Dr. Kay as a product of his own work and not a product of the work of any of the other inventors listed on the Snyder patent.

Nevertheless, Applicant has shown an absence of a reasonable expectation of success of combining Snyder with Kurachi, along with unexpected results that were obtained from the expression cassettes of the present invention, as discussed in the response filed March 8, 2006, and in the attached declaration by Dr. Mark Kay. Applicant refers the examiner to the attached 37 CFR §1.132 declaration by Dr. Mark Kay that was submitted with this response stating that, based on the information available at the time the present application was filed, one of skill (1) could not reasonably expect that the addition of an intron would enhance transgene expression in the case of in vivo delivery of a transgene into post-natal animals; (2) could not reasonably expect that any

particular promoter would perform better under in vivo conditions based on in vitro studies; (3) could not reasonably expect that an expression cassette, such as the expression cassette of claim 1 having a combination of an intron and a heterologous promoter, would increase transgene expression nearly 100-fold in vivo when given to post-natal animals, particularly since there was almost no enhancement with in vitro transgene expression in cultured hepatocytes and a hepatoma cell line. Moreover, Applicant alerts the examiner to the statement at paragraph 10 of the declaration made by Dr. Kay, which is directly relevant to the examiner's position at page 5 of the present action regarding unexpected results, stating that there is no significant influence on transgene expression in vivo in post-natal animals when the expression cassette is constructed without the untranslated region located 3' to the coding region and the intron.

Furthermore, the attached declaration still makes it clear (1) that the examiner would have to resort to improper hindsight reasoning to argue that the present invention is obvious over Snyder (as evidenced by Simonet and Nguyen) in view of Jallat and Kurachi, (2) that there is an absence of a reasonable expectation of success in producing the claimed construct; and (3) that the art itself teaches away from combining Kurachi with Snyder, since one of skill in this art would certainly be aware of the teachings of Brinster and Palmiter, as well as that of Dr. Kay, as discussed in the attached declaration. These teachings show, respectively, that the introns substantially enhanced transgene expression in transgenic mice but not tissue culture cells because of the developmental alteration of the genes in the transgenic mice, and exogenous expression cassettes are regulated differently in cultured primary hepatocytes when compared to in vivo in a liver. Therefore, the combined teachings would teach one of skill away from simply combining the introns of Kurachi with the construct of Snyder to further enhance transgene expression.

In view of the above, Snyder can no longer be considered a prior art reference. Irregardless of Snyder's status as prior art, Snyder did not provide a way for one of skill, at the time of filing the present application, to predict with any reasonable expectation of success (1) which promoters would perform better under in vivo conditions based on in vitro studies and (2) whether there would be any in vivo enhancement of expression using the intron of Kurachi combined with any such promoter. Moreover, the unexpected results in enhanced expression observed with the present invention further obviate the examiner's assertion that the expression cassette of the present invention is obvious in view of any of the cited art. Accordingly, Applicant respectfully requests that the rejection of claims

1-4 and 16 be withdrawn for at least these reasons.

Conclusion

In view of the foregoing, a Notice of Allowance is respectfully requested for claims 1-4, 15, 16, 24, and 36-43. If the examiner has any questions or believes a telephone conference would expedite prosecution of this application, the examiner is encouraged to call the undersigned at (650) 838-4388.

Respectfully submitted,
Perkins Coie LLP

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Brian S. Boyer, Ph.D.
Registration No. 52,643

Correspondence Address:
Customer No. 22918